ALBERTA HERITAGE FOUNDATION FOR MEDICAL RESEARCH

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RESEARCH
OUTSIDE THE LAB

How children acquire language is one of many Heritage research projects "outside the lab"

On the Cover

The cover and feature story photos were shot by Calgary photographer Trudie Lee whose work is regularly featured in *AHFMR Research News*.

research news

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SPRING 2006

5 **Staying alive: viruses and the immune system**

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6 **Stroke: brain attack**

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Research outside the lab

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AHFMR Mission

AHFMR supports a community of researchers who generate knowledge whose application improves the health and quality of life of Albertans and people throughout the world. AHFMR's long-term commitment is to fund health research based on international standards of excellence and carried out by new and established investigators and researchers in training.

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Regenerative medicine is an emerging scientific field geared toward offering new solutions to such age-old illnesses as Alzheimer's, cancer, diabetes, and cardiovascular disease. The field spans many scientific disciplines, using a combination of stem-cell biology, gene therapy, and tissue-engineering. Although these new technologies may offer the potential to treat a number of chronic diseases, some elements of regenerative medicine are steeped in controversy.

The bioethics of regenerative medicine

University of Toronto bioethicist Dr. Abdallah Daar is involved in research ranging from bioindustry ethics to nutritional genomics, but he is particularly passionate about regenerative medicine. Realizing the full power of regenerative medicine and ensuring its ethical use is the daunting task Dr. Daar and his colleagues face. Many of the objections that have been raised about stem-cell research also affect regenerative medicine.

Stem cells are undifferentiated cells in the human body that have the ability to become any type of specialized cell—bone, for example, or muscle, or cartilage. Because of this ability, stem cells have the potential to treat many diseases. Stem cells may even have the power to regenerate organs, thereby reducing the need for transplants and other serious surgeries. The early embryo is one source of stem cells, leading some to question the morality of using these cells for research; but Dr. Daar points out that stem cells can be harvested from a number of different sources. "The science is really progressing rapidly, and one day it may be possible to take specialized cells, such as skin cells, from the adult and reprogram them back to stem cells."

"Science and technology is one way to channel the resources of the developing world."

Harnessing the power of regenerative medicine

Dr. Daar believes that one of the most valuable opportunities for regenerative medicine lies in developing nations. "We think of diabetes, cardiovascular disease, and cancer as so-called 'Western diseases', when this isn't the case," he explains. "Diabetes is increasing rapidly; 80% of global cardiovascular disease is arising from developing nations; and cancer rates are expected to increase dramatically. Diabetes, cardiovascular disease, and cancer are chronic diseases, which translates into the fact that they are expensive to treat. If you live in a developing nation that doesn't have the resources to manage these diseases, it can be tantamount to a death sentence." Regenerative medicine technologies may offer a viable, cost-effective solution for managing many of these diseases. Furthermore, the involvement of developing nations in the research and implementation of technologies may reduce their reliance on technology imports—while also creating jobs.

ABOVE: DR. ABDALLAH DAAR

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Overcoming the hurdles

One of the overarching themes at the University of Toronto Joint Centre for Bioethics is that its members do not study "bioethics as usual"—theoretical bioethics. "The goal of our organization is to get involved in the real world," explains Dr. Daar. "We perform large-scale research projects and get involved with the policy-makers to make it likely that realistic policies are related to science and technology. Developing countries have great health needs, and we have an obligation to attempt to reduce global health inequities. Identifying potential scientific and technological approaches to improve health is one avenue for making a difference. Science and technology will not solve all problems—such as poor governance or corruption—but it is one way to channel the resources of the developing world."

Dr. Abdallah Daar is a professor in the departments of Public Health Sciences and Surgery at the University of Toronto. He is also the director of the Program in Applied Ethics and Biotechnology at the Joint Centre for Bioethics; the director of the Ethics and Policy Program at the McLaughlin Centre for Molecular Medicine; and a co-director of the Canadian Program on Genomics and Global Health, all at the University of Toronto. Dr. Daar gave the lecture "Whither regenerative medicine?" as part of the University of Alberta Health Law Institute's 2005-2006 seminar series.

AHFMR frequently receives letters requesting information about Heritage research or about various medical conditions. "Responding to the Reader" is an *AHFMR Research News* feature intended to provide up-to-date information related to readers' questions, with the help of experts in the Alberta research community. AHFMR cannot provide medical advice, however; please see your family physician about your specific health concerns.

> *Hemochromatosis* is a condition in which the body absorbs too much iron from the diet, resulting in a buildup of iron in organs and tissues. If untreated, the disorder can result in such significant complications as cirrhosis, diabetes, and congestive heart failure. One in 227 Canadians of northern European descent has a genetic predisposition to hemochromatosis, making it the most common genetic disorder in North America. A reader has asked whether too much iron in the body may cause cancer, a possibility which would certainly be of concern, not only to those with hemochromatosis, but also—because so many foods today are iron-fortified—to the general public.

Dr. Dawna Gilchrist is a clinician-teacher at the University of Alberta who specializes in genetic disorders of adult onset, including hereditary cancers. She says there is no evidence that iron causes cells to become cancerous. "Iron is a cellular toxin," she explains. "It can cause cell death. If you've got death of heart cells, you've got heart failure; if you've got death of pancreatic cells, you've got diabetes; and death of liver cells can cause cirrhosis. Iron kills cells; it doesn't transform them into cancer." Dr. Gilchrist adds that the only instance where iron could be linked to cancer is in hepatocellular carcinoma, a type of liver-cell cancer, but this rare cancer may occur in anyone with cirrhosis, not just someone with advanced hemochromatosis. The cancer is related to cirrhosis, not specifically to iron.

Hemochromatosis is a relatively common disease with a variety of potential symptoms. "People who have a genetic predisposition sometimes assume that all of their health problems are related to that genetic issue; however,

Hemochromatosis is a relatively common disease

"Iron kills cells; it doesn't transform them into cancer"

"There are people who have this genetic pattern their whole lives and never get adverse effects," explains Dr. Adams. "There is a huge spectrum of clinical presentation. We're now trying to correlate some of the symptoms that might be related to iron overload with the various genetic patterns to learn more about this."

this isn't necessarily the case," says Dr. Gilchrist. For example, a patient might have both hemochromatosis and lung cancer–but the lung cancer would be associated with smoke exposure, not with iron toxicity. They are simply independent disorders.

Patients may also assume that, because they have a genetic predisposition to store too much iron, they will develop health problems. However, a predisposition is just that. In order for damage to occur to the body, other factors (such as too much iron in the diet, overuse of alcohol, or viral hepatitis) must come into play. In a recent study by the University of Western Ontario's Dr. Paul Adams, more than 100,000 people were screened for iron overload. Of those whom he found to have the typical genetic pattern for hemochromatosis–at the typical rate of 1 in 227 Caucasians–many had no apparent illness at all.

Dr. Dawna Gilchrist is an associate professor in the Division of General Internal Medicine within the Department of Medical Genetics at the University of Alberta. She is in the process of developing clinical-practice guidelines for the diagnosis and management of genetic hemochromatosis.

Dr. Paul Adams is a professor in the Department of Medicine's Division of Gastroenterology at the University of Western Ontario. He received funding from the National Institutes of Health (NIH) in the United States for the Hemochromatosis and Iron Overload Screening Study (HEIRS).

Selected publication

Adams PC, Reboussin DM, Barton JC, McLaren CE, Eckfeldt JH, McLaren GD, Dawkins FW, Acton RT, Harris EL, Gordeuk VR, Leiendecker-Foster C, Speechley M, Snively BM, Holup JL, Thomson E, Sholinsky P. Hemochromatosis and iron-overload screening in a racially diverse population. *New England Journal of Medicine* 2005 Apr 28;352(17):1769-1778.

The cells of our body may hold the key to understanding how allergic diseases such as asthma and rheumatoid arthritis work. AHFMR Scholar Dr. Gary Eitzen is spreading the news that knowing how cells work can have important implications for treating allergic inflammation.

Cellular construction

Dr. Eitzen is an energetic scientist who talks with ease about his intricate research on cellular proteins known as *small monomeric G proteins*. "I like to think of G proteins as the foremen of the cells," he begins. "If the foreman on a building site gets a call to finish the fifth floor, he tells the workers below him to get the job done. G proteins function in much the same way—in that they receive a 'phone call' from the surface of the cell that tells them to build something, and they signal to factors downstream to get the job done."

Analogy aside, G-protein function is quite complex, as these tiny proteins perform many functions. G proteins can do everything from inducing cellular growth to increasing communication between cells; they can also tell cells to secrete substances such as hormones and enzymes into their environment. Dr. Eitzen's research focuses on how G proteins function in the cell secretion which is important during an immune response.

G-proteins are the foremen of the cells

"There are times when secretion is good," he explains, "for instance, during a bacterial infection. The cells of the body secrete enzymes and antibodies to help fight the infection. In the case of allergic inflammation, secretion is bad because the cells are secreting enzymes when there is nothing there to fight. We ask a number of questions, such as: Who is making the call to the G protein? What G protein is taking the call, and what does the protein then do?" Learning the answers to these questions is helping Dr. Eitzen figure out how cells respond to allergic inflammation. This research can then be translated into better allergy therapies.

His excitement is apparent when he talks about some of his recent discoveries. "One of the things we've found is that G proteins are involved in remodelling the cellular architecture known as the cytoskeleton. When the G proteins receive a signal to secrete, they basically move structures around so that it can be done effectively. When it comes to dealing with allergic inflammation, we may be able to target the cytoskeleton. If we can stop specific cytoskeletal rearrangement, we may be able to stop secretion and effectively block allergic inflammation."

Dr. Eitzen credits much of his success to the research environment at the University of Alberta. There is no hesitation in his voice as he talks about why he loves his career. "I am very much a bench scientist. I like to play with the toys in the lab and work on the bench. Having the ability to hand out projects to students and to actively work on those projects with them is very rewarding." He also notes that the students are exceptionally innovative. "The calibre of students here at the University of Alberta is excellent, and I believe we have the best cell-biology program in the country because of it."

AHFMR Scholar Dr. Gary Eitzen is an assistant professor in the Department of Cell Biology at the University of Alberta. *Dr. Eitzen's work is also supported by the Canadian Institutes for Health Research (CIHR) and the AllerGen Allergy, Genes and Environment Network of Centres of Excellence.*

Selected publication

Tedrick K, Trischuk T, Lehner R, Eitzen G. Enhanced membrane fusion in sterol-enriched vacuoles bypasses the Vrp1p requirement. *Molecular Biology of the Cell* 2004 Oct;15(10):4609-4621.

DR. GARY EITZEN

STAYING ALIVE

VIRUSES AND THE IMMUNE SYSTEM

HOW DO VIRUSES TURN OFF THE BODY'S EARLY-WARNING IMMUNE SYSTEM? THIS IS THE KEY QUESTION FOR AHFMR SENIOR SCHOLAR DR. MICHELE BARRY, AND THE ANSWERS AND THEIR IMPLICATIONS ARE SURPRISINGLY COMPLEX.

"The body is able to ward off infections quite effectively by means of the innate immune system–the body's first line of defence when it comes to fighting off foreign invaders," explains Dr. Barry. "Innate immunity recognizes non-specific foreign bodies and attacks them. Basically, it keeps breaches at bay until the body can determine what it's dealing with and mount the appropriate full-scale immune attack against it." This full-scale counterattack involves the adaptive or acquired immune system, which provides long-lasting, specific protection, but which takes longer to swing into action.

If the innate immune system doesn't work properly, there can be dire consequences. Many viruses have developed the ability to escape detection by the innate immune system, allowing them to replicate and infect their host unchecked. "The nature of my research is two-fold," says Dr. Barry. "I want to understand how viruses evade immune detection and, based on this, dissect the antiviral pathways used by the immune system. Usually, when a cell becomes infected, it sends out big red flags that signal to the body's immune system: 'I'm infected!' The innate immune system then seeks out the infected cell and sends signals that cause it to die. This form of cell death is known as apoptosis."

MANY VIRUSES HAVE DEVELOPED THE ABILITY TO ESCAPE DETECTION

The many pathways and proteins within the cell that turn on and shut off apoptosis make the process challenging to study. Although the infected cell may receive a signal from the innate immune system telling it to die, the virus may have the ability to produce proteins that block this signal. Dr. Barry's team has discovered a protein known as F1L, made by the poxvirus vaccinia. F1L works to shut off the apoptotic pathway at a pivotal point, so that the host cell containing the virus does not die as it should. This allows the virus to continue replicating and infecting other cells in the body.

Understanding how viruses work could be the key to improving treatment. Dr. Barry's research could also help us understand more about cancer, since apoptosis is often turned off or down-regulated in cancerous cells.

The University of Alberta and AHFMR are not the only organizations to recognize the potential impact of her work. In 2004, Dr. Barry was one of five Canadians who received a prestigious Howard Hughes International Research Scholar award. Not only is the award a huge honour; it will also help fund Dr. Barry's research for the next five years. "I am thrilled about the recognition, and I know the support system that surrounds me here at the University of Alberta is a key contributor to my laboratory's success," says Dr. Barry.

AHFMR Senior Scholar Dr. Michele Barry is an associate professor in the Department of Medical Microbiology and Immunology at the University of Alberta, and a Howard Hughes International Research Scholar in Infectious Diseases. Dr. Barry's work is also supported by the Canadian Institutes of Health Research (CIHR). She is the recipient of a Boehringer Ingelheim Young Investigator Award.

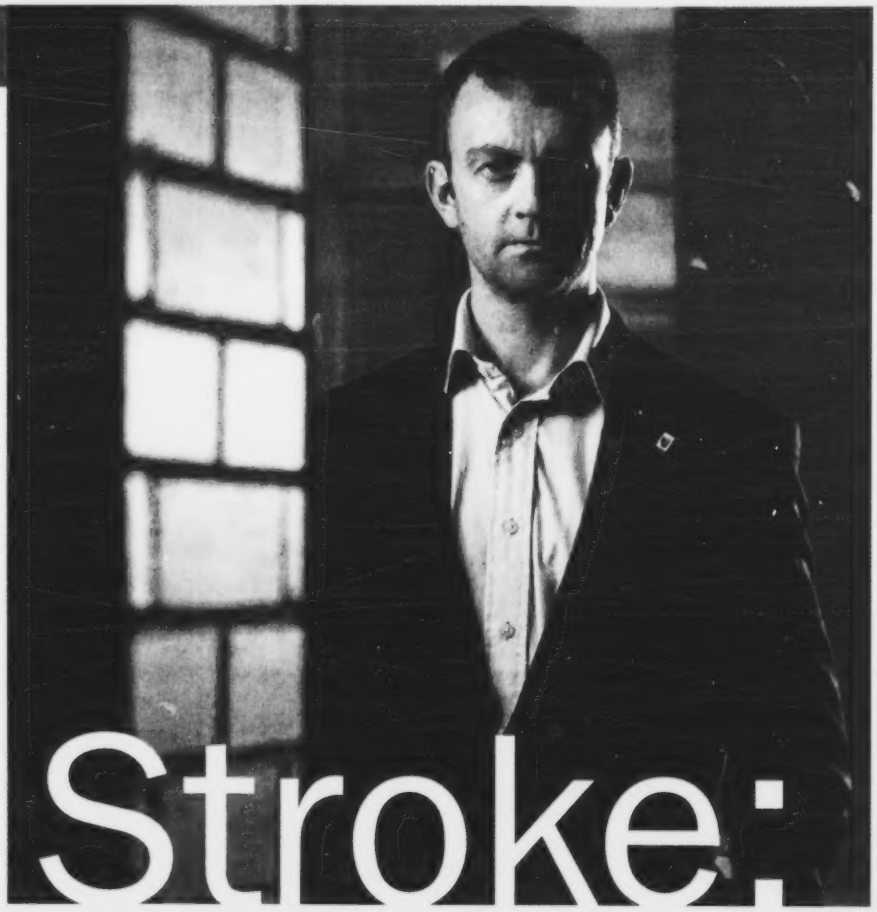
Selected publications

Stewart TL, Wasilenko ST, Barry M. Vaccinia virus F1L protein is a tail-anchored protein that functions at the mitochondria to inhibit apoptosis. *Journal of Virology* 2005 Jan;79(2):1084-1098.

Wasilenko ST, Stewart TL, Meyers AFA, Barry M. Vaccinia virus encodes a previously uncharacterized mitochondrial-associated inhibitor of apoptosis. *Proceedings of the National Academy of Sciences* USA 2003 Nov 25;100(24):14345-14350.

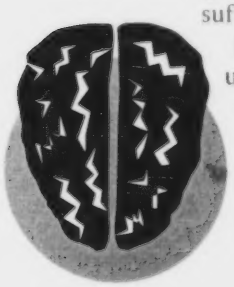
RIGHT: DR. MICHELE BARRY

In the depths of the Health Sciences Building at Calgary's Foothills Medical Centre, researchers from various disciplines investigate the structural and functional changes that occur in disease. The Experimental Imaging Centre (EIC) provides access to Canada's largest Tesla magnet for magnetic resonance (MR) and optical imaging, in order to investigate ways to improve the diagnosis, monitoring, and treatment of medical disorders.



Stroke: brain attack

Heritage Clinical Investigator and neurologist Dr. Philip A. Barber conducts stroke research in the EIC, as well as stroke diagnosis and care in the Seaman Family MR Research Centre and the Hotchkiss Brain Institute. *Stroke* is a sudden loss of brain function caused by the interruption of blood flow to the brain, through either *ischemia* (blood-vessel blockage) or *hemorrhage* (blood-vessel rupture). In Canada, stroke is the single most common cause of neurological disability and death; 5,000 strokes occur every year in Alberta alone. If you live to the age of 80, you have a 1-in-4 chance of suffering a disabling stroke.



Early treatment can be very beneficial; unfortunately patients often do not recognize the warning signs of stroke—such as loss of speech, loss of motor skills, and loss of vision—and are slow to seek diagnosis and treatment. A clot-busting drug called tissue plasminogen activator (tPA) can improve the outcome of acute ischemic stroke; but few stroke patients are eligible, since the treatment must be administered quickly.

"In Calgary, we're treating about 10% of all strokes with tissue plasminogen activator, but we'd like it to be 20%," says Dr. Barber. "In the United States they treat about 1% of all strokes with tPA. Calgary is doing better than most places in the world, but we could do better."

Some patients experience significant side effects with tPA. Researchers believe that these adverse effects are strongly related to the initial breakdown of the *blood-brain barrier*—the membrane that controls the passage of substances from the blood into the central nervous system. Current imaging techniques for the brain in stroke cannot predict which patients are susceptible to the side effects. Dr. Barber—in collaboration with chemists, physicists, biologists, molecular biologists, and clinicians—studies the blood-brain barrier.

ABOVE: DR. PHILIP A. BARBER

5,000 strokes occur every year in Alberta

The breakdown of this barrier is one of the first things to happen in stroke, he explains. "If we could understand this process better, we could target various treatments; and also, with the imaging, we could actually define whether our therapeutic intervention had any effect," says Dr. Barber.

"Whilst we're working in research and trying to answer academic questions, the questions are essentially relevant to stroke patients," he points out. "What we intend to do is to translate information from bench to bedside. This environment is quite novel. There are people like myself working alongside basic scientists from all fields, and down the corridor I can be seeing a patient in five minutes. We have the capacity to take information from the Experimental Imaging [Centre] over to the Seaman Family MR Centre for clinical application.

Patients often do not recognize the warning signs of stroke

"We're at the beginning of our research," he continues. "There's much work to do, but it's exciting to have an idea, design a study, collect the data, and do the analysis. Sometimes your question will provide an answer which may be novel and which may potentially provide a new understanding of stroke, and ultimately a novel therapy."

Dr. Philip Barber is a Heritage Clinical Investigator and an assistant professor in the Department of Clinical Neurosciences, as well as a Clinical Stroke Fellow in the Calgary Stroke Program at the University of Calgary. He receives research support from the Heart and Stroke Foundation of Canada and the Canadian Institutes of Health Research (CIHR). Dr. Barber is also a member of the Hotchkiss Brain Institute.

The University of Calgary Faculty of Medicine, in a unique collaboration with the NRC (National Research Council Canada) Institute for Biodiagnostics and AHFMR, provided funding for the Experimental Imaging Centre (EIC) and its ultra-high-field 9.4-Tesla MRI system.

Selected publications

Barber PA, Foniok T, Kirk D, Buchan AM, Laurent S, Boutry S, Muller RN, Hoyte L, Tomanek B, Tuor UI. MR molecular imaging of early endothelial activation in focal ischemia. *Annals of Neurology* 2004 Jun 28;56(1):116-120.

Barber PA, Demchuk AM, Zhang J, Buchan AM. Validity and reliability of a quantitative computed tomography score in predicting outcome of hyperacute stroke before thrombolytic therapy. *Lancet* 2000 May 13;355(9216):1670-1674.

What is a stroke?

A stroke is a sudden loss of brain function caused by the interruption of blood flow to the brain (an *ischemic* stroke) or the rupture of blood vessels in the brain (a *hemorrhagic* stroke). Both types of stroke cause brain cells (neurons) in the affected area to die. The effects of a stroke depend upon where the brain was injured, as well as how much damage occurred. A stroke may affect

- ability to move and coordinate movement;
- ability to feel touch, temperature, pain, and movement;
- ability to see or to interpret what you see;
- ability to think, remember, understand, plan, reason, or problem-solve;
- ability to communicate (speaking and understanding speech, as well as reading, writing, and the ability to do mathematics);
- personality;
- emotions;
- behaviour.

What is a "mini-stroke"?

A "mini-stroke" is a transient ischemic attack (TIA) caused by a temporary interruption of blood flow to the brain. TIA symptoms are similar to those of an ischemic stroke, except that they go away in a few minutes or hours (no more than 24 hours). A TIA is an important warning sign that you may be at risk for an ischemic stroke in the future.

What are the warning signs of stroke?

Learn to recognize the warning signs of a stroke:

Weakness – sudden weakness, numbness, or tingling in the face, arm, or leg

Trouble speaking – sudden temporary loss of speech, or trouble understanding speech

Vision problems – sudden loss of vision (particularly in one eye), or double vision.

COURTESY: HEART AND STROKE FOUNDATION OF CANADA


"THE VALUE OF THIS RESEARCH IS IN DISCOVERING WHAT WORKS IN THE REAL WORLD"

RESEARCH
OUTSIDE THE LAB

REAL LIFE IS COMPLICATED. That's a given for all of us, but it can make certain types of research particularly tricky to conduct. Take Calgary psychologist Dr. Shervin Vakili's research into binge drinking on campus. He is testing two types of intervention aimed at curbing this problem (see sidebar). Like any scientist, he has identified a population to study; he has placed his research subjects into groups according to the intervention they will receive; and he will evaluate whether the interventions have made a difference in behaviour.

"The problem is that I can't control the other variables during the two years this study will run," says Dr. Vakili. "For example, there may be a crack-down on student drinking, a new law may be passed, or a new bar may open on campus. All these things would make it more difficult to determine the exact effects of the interventions. On the other hand, if I try to control the variables, then it's not real life any more and the external validity of the results would be questioned. The value of this sort of research is in discovering what works in the real world. The trick is to set up your study in such a way as to control for as many of the real-life variables as possible while still maintaining a natural environment."

That's one of the challenges of doing health research outside the lab, and it's irresistible for many Alberta researchers. "This type of research is not easy, it's time-consuming and expensive, and you have to follow people for a number of years before you get answers," says Dr. Vakili. "But, to tell you the truth, I wouldn't have it any other way. This is really exciting."

In the following article we take a look at eight AHFMR researchers who are working outside the lab on unusual research projects.

ABOVE: DR. SHERVIN VAKILI

ALTERNATIVE THERAPIES LEADING THE WAY

WITH MORE THAN 50,000 natural health products available in Canada, and widely varying claims about their effectiveness, it's hard to know what to think about complementary and alternative-medicine (CAM) therapies. And doctors face the same dilemma as the rest of us.

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"Suppose I'm considering using melatonin (a hormone that is sold without a prescription in health-food stores and drug stores) to treat insomnia in a child with attention deficit disorder," says Edmonton pediatrician and Heritage Population Health Investigator Dr. Sunita Vohra. "How do I know whether it's effective or not? And if it is, what dose should I recommend?"

Doctors can refer to the results of randomized clinical trials—the gold standard for evaluating treatment efficacy—but those results are not necessarily applicable to the individual patient in front of them. Using Dr. Vohra's example, while there may have been a clinical trial on the effectiveness of melatonin, it probably would have excluded participants with pre-existing conditions such as attention deficit disorder. So the results would not necessarily apply to her patient. A complicating factor for many complementary therapies is that randomized clinical trials have not yet been done. Dr. Vohra investigates another way to assess pediatric CAM therapies—an "N-of-1" trial (N being the letter normally used to designate a population of subjects taking part in an experiment).

"WE WRAP THE RESEARCH METHODS AROUND THE PATIENT"

N-of-1 trials evaluate the effectiveness of a procedure or treatment in a single person, rather than a larger number of subjects. "An N-of-1 trial evaluates the individual's potential for benefiting from a specific treatment," explains Dr. Vohra, who has had training in pharmacology and epidemiology, as well as medicine. "Instead of putting the patient into a research model, as we do in a randomized controlled trial, we wrap the research methods around the patient.

"We think N-of-1 is a particularly good approach to sifting through the huge number of CAM therapies, many of which are used for multiple conditions. It's a way to find the therapies that appear to be helpful and are therefore worth additional attention."

Dr. Vohra heads the Complementary and Alternative Research and Education (CARE) program at the Stollery Children's Hospital, Canada's first academic program in pediatric integrative medicine (the combination of conventional and alternative treatments). With support from a number of partners, her team has embarked on an ambitious multi-phase project that aims to develop a rigorous approach to evaluating and pooling the results from N-of-1 trials. It will establish an N-of-1 registry at the Stollery Children's Hospital, develop guidelines for the reporting of N-of-1 trials, and set up a pharmacy service to create natural health products for trials and test them for stability.

"I believe we have to keep an open mind about CAM therapies," she says. "There is so much we don't know. By putting the needs of patients first, as is done in N-of-1 trials, we can learn."

SABINE MORITZ has been conducting research on CAM therapies since 1998. She is the research director of the Canadian Institute of Natural and Integrative Medicine (CINIM) in

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ABOVE: DR. SUNITA VOHRA
RIGHT: SABINE MORITZ

Understanding language impairment

Language impairment can have a profound effect on a child's life. For example, a developmental language disorder called Specific Language Impairment (SLI) makes it very difficult to learn to read, and generally hampers a child's academic success. Early intervention can help; and schools now focus on diagnosing children with SLI.

But our desire to help may actually be hurting some students. Children who are learning English as a second language (ESL) tend to make mistakes similar to those that monolingual children with SLI make. For example, both ESL children and monolingual children with SLI might say "he go over there" instead of "he goes over there".

"As a result of these kinds of errors, children learning ESL can get caught in the net of being falsely labelled as language- and learning impaired," says Heritage Population Health Investigator Dr. Johanne Paradis, a linguistics professor at the University of Alberta. "The problem stems from the fact that our assessment tools are normed to a monolingual population. There is virtually nothing for children whose native language is not English."

The long-term objective of Dr. Paradis is to develop such tools. Her first step was to investigate the typical errors made by ESL children, and compare them to ones made by children with SLI. The research team followed children learning ESL who came from a variety of language backgrounds, including Arabic, Spanish, and Mandarin. For two and a half years, they were regularly given tests to evaluate comprehension and production of English—the kind of tests used to detect language impairment.

"The results are a good-news bad-news story," says Dr. Paradis. "The bad news is that there is a huge amount of overlap in the kinds of errors children make. What's worse is that, even after more than two years, the children learning ESL still scored as language-impaired. This isn't a temporary thing; it takes them a long time to perform as a native speaker does. The good news is that there are some small differences in the way children learning ESL make these errors."

To follow this up, Dr. Paradis is hoping to start a large-scale study that would recruit and test hundreds of children learning ESL—children from different language backgrounds, of different ages, and with different levels of exposure to English. "There were only 24 children in my first study. Because individual variation is so high, we need large numbers to develop norms for children learning ESL. In this way I hope to turn an academically interesting finding into a clinically relevant tool."

Dr. Johanne Paradis is an AHFMR Population Health Investigator and associate professor in the Department of Linguistics, part of the Faculty of Arts at the University of Alberta. Her research is supported by the Social Sciences and Humanities Research Council of Canada.

ABOVE: DR. JOHANNE PARADIS

Help for overweight children

National surveys have revealed that the number of overweight youth in Canada has increased dramatically over the past couple of decades. Currently in Alberta, about one in four children is overweight.

"Right now, children are facing very real health risks from being overweight," says Heritage Population Health Investigator Dr. Geoff Ball, a registered dietitian who is one of Canada's leading specialists in pediatric obesity. "Currently there's precious little to offer families. There are programs that are simply modified versions of adult interventions; but the design, delivery, and evaluation of these programs often doesn't fit a pediatric model."

Dr. Ball notes that while placing a child on a 1200-calorie diet and prescribing a structured exercise plan can cause weight loss, there is limited sustainability over the long term. "With traditional weight-loss strategies, weight loss is usually *the* indicator of success. We are developing, delivering, and evaluating novel programs that target a host of quantitative and qualitative outcomes to evaluate health improvements in families and the effectiveness of our team in health services delivery. We want to do better for our children and families, and our practice-based research clinic will facilitate ongoing program evaluation."

Dr. Ball heads Capital Health's Pediatric Centre for Weight and Health (PCWH) at the Stollery Children's Hospital in Edmonton, the first centre of its kind in Canada to fully integrate weight-management care and research in pediatric obesity. One of the centre's current projects is the development and evaluation of a new weight-management program for overweight 13- to 17-year-olds. The HIP (Healthy Initiatives Program) for Youth intervention addresses weight-related issues by combining cognitive behavioural therapy and motivational interviewing strategies.

Teens attend counselling sessions over 20 weeks; support and follow-up are provided through the PCWH for an additional two years. Counselling involves individual coaching from "HIPmates", roles taken on by the PCWH dietitian, exercise specialist, and nurse. Not only are they experts on lifestyle behavioural counselling and weight-related issues; HIPmates are specially trained in communicating with teens and their families. Capitalizing on the emerging independence of teenagers, the one-on-one sessions with HIPmates aim to understand the causes of the teen's weight and explore strategies to support healthy behavioural changes.

Outcomes for participants in the HIP for Youth program will be compared to those for the young people who participate in the Youth Lifestyle Program—which takes a more traditional weight-loss approach—and those for a control group (teens on the wait list). Enrolment in the study began in January 2006 and will continue over the next two years. A new, family-centred program for overweight 8- to 12-year-olds and their parents will begin in the spring.

"The PCWH offers a great opportunity for treatment and research, but we also have an important role to play by increasing pediatric weight-management capacity among students, health professionals, and researchers," Dr. Ball adds. "By increasing the knowledge and skill base, we can help a far greater number of people than we will ever see through our clinic doors."

Dr. Geoff Ball is an assistant professor in the Department of Pediatrics at the University of Alberta, and director of Capital Health's Pediatric Centre for Weight and Health (PCWH) at the Stollery Children's Hospital. An AHFMR Population Health Investigator, he receives support for his research from the Canadian Institutes of Health Research (CIHR) and the Stollery Children's Hospital Foundation.

Selected publication

Ball GDC, Huang TT-K, Gower BA, Cruz ML, Shaibi GQ, Weigensberg MJ, Goran MI. Longitudinal changes in insulin sensitivity, insulin secretion, and β-cell function during puberty. *Journal of Pediatrics* 2006 Jan;148(1):16-22.

ABOVE: DR. GEOFF BALL

Calgary. One of her most recent projects is a study on the benefits of a program teaching spirituality to people suffering from depression.

The impetus comes from the results of a previous study done by CINIM that examined the effect of a spirituality program and a mindful-meditation program on mood states. The people who took the spirituality program showed a 46% reduction in total mood disturbance, compared to a 26% reduction in the meditation group and an 11% reduction in the control group.

A number of sub-scores were also analyzed, and the depression score was found to be particularly improved in the spirituality group. The finding immediately piqued the research team's interest, says Ms. Moritz. "The results started us thinking: Could the spirituality program be used as a treatment for depression?"

The new study is a randomized controlled trial to assess whether the spirituality program is effective in reducing the severity of depression (improving response rates, remission rates, and quality of life), and whether the efficacy is maintained long term. Participants are first assessed by a psychiatrist, and only those diagnosed with major depression may enter the trial.

The spirituality teaching aims to improve mood and quality of life by presenting insights on meaning and purpose, connectedness and values. An eight-week, home-based program on CDs, it consists of eight 60- to 90-minute teaching sessions and a daily 15-minute visualization exercise. The program avoids focusing on any particular religion and is suitable for people with various cultural backgrounds. It was developed by psychiatrist Dr. Badri Rickhi, CINIM's research chair.

"THERE'S AN ASPECT TO DEPRESSION THAT DOESN'T RESPOND TO CONVENTIONAL THERAPY"

CINIM hopes to complete recruitment for the study by May 2006. (For details on how to participate in this study, go to www.cinim.org.) Ms. Moritz is eager to see the results. "Depression is often viewed as a strictly biochemical disorder. Antidepressants that treat the chemical imbalance can be effective, but they don't work for everyone. There's an aspect to depression that doesn't respond to conventional therapy. If this aspect is addressed effectively, perhaps it can truly help people with depression change their lives."

ABOVE: DR. JOHN MCLENNAN

HELPING VULNERABLE POPULATIONS

IN MEDICAL SCHOOL Dr. John McLennan felt he was being pulled in two different directions: public health and child psychiatry. Rather than choose between them, he decided to do both—he took research training in public health and did a clinical specialty in child psychiatry. Now a Heritage Population Investigator at the University of Calgary, Dr. McLennan is putting together a research program that embraces both worlds. His interest is in the life trajectories of high-risk children and youth, and society's efforts to improve those trajectories. He studies children with fetal alcohol syndrome and attention deficit hyperactivity disorder, malnourished children, and those who are in conflict with the law.

"Children with developmental, mental-health, and social problems are in programs across many sectors—social services, the health system, the mental-health system, and the educational system. I want to know about the outcomes of these programs, what society is doing to improve outcomes, whether society is using evidence-based interventions to improve outcomes, and whether those attempts have been effective."

Sounds straightforward? It's not. "It's a mess to try to figure out what services are being offered and who is getting them," says Dr. McLennan. "Record-keeping is not good. There's no common database."

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From examining projects in Canada, the Caribbean, and South America, he has discovered at least one common theme: for the majority of services in most sectors, providers are not using evidence-based interventions. Instead of effectiveness, the basis for choosing interventions tends to be theoretical understanding, preference of the service provider, and cost.

"What this means is that children are receiving interventions, and we don't know whether they're effective, ineffective, or harmful," says Dr. McLennan. "People forget that psychosocial interventions can have adverse effects just as medical treatments do. Interventions can do harm; it's not simply a matter of 'something is better than nothing'."

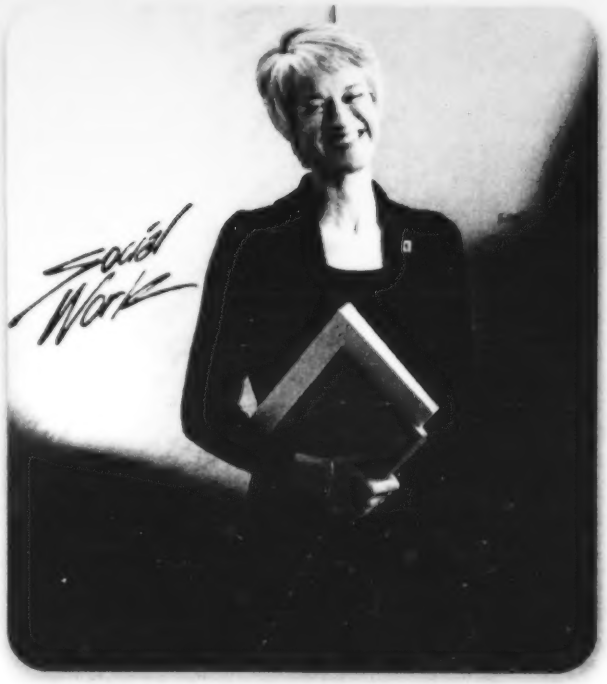
"PEOPLE FORGET THAT PSYCHOSOCIAL INTERVENTIONS CAN HAVE ADVERSE EFFECTS"

The other missing piece is measurement of outcomes. "It's amazing that, although society is investing in helping high-risk children, outcome data are rarely collected. Although people talk about outcomes, they collect utilization data instead, which tell us how many people used the service, but not much else. This area is so grossly underevaluated."

Little by little, Dr. McLennan says, the message of evidence-based interventions is getting through. McMaster University in Ontario has been a leader in this area. The recent establishment of the Population Mental Health Research Program at Calgary's Hotchkiss Brain Institute is the beginning of an Alberta-based cluster of expertise.

"There's a huge opportunity here. I believe that it's better to know than not know about how effective services are. We can't move forward if we just keep offering services without evaluating them."

In the Faculty of Social Work at the University of Calgary, another Population Health Investigator also studies vulnerable populations. Dr. Catherine Worthington's research involves understanding the needs of vulnerable groups, such as street youth and Aboriginal youth, and designing services for them that will provide the best quality of care possible. For example, social services that are designed from a middle-class, nine-to-five perspective are probably not going to meet



the needs of a young person who lives on the street. Access is likely to be a problem; the program environment might not be inviting; and the services themselves may not be what the street youth really needs.

Dr. Worthington is particularly interested in groups that are vulnerable to HIV, the virus that causes AIDS. "In Canada, HIV has become a disease of vulnerable populations," she notes. "The cultures and lifestyles of vulnerable populations have not been recognized by the mainstream. Although HIV is a huge risk in these communities, services are not designed for them.

"IN CANADA, HIV HAS BECOME A DISEASE OF VULNERABLE POPULATIONS"

"HIV is a virus that is transmitted via interactions between people. So the way to understand HIV in terms of prevention—and also use of treatment—is to look at the social environment. This means finding out how street youth interact among themselves, finding out what it's like for an Aboriginal youth to go for HIV testing. You have to step out of your own shoes."

One of Dr. Worthington's current studies investigates the services available to street youth in Calgary. Working with youth organizations,

ABOVE: DR. CATHERINE WORTHINGTON

health-service agencies, and street kids themselves, her team developed a questionnaire to identify the factors that promote or impede the use of services relating to HIV and other health issues. The survey of 350 street-involved youths is now being followed up with 40 personal interviews to get in-depth information from young people in different social groups and sub-groups.

"We've already done some of the interviews and I've read through the transcripts," says Dr. Worthington. "These kids lead very complicated, challenging lives, but they also show great strength and resiliency. The problem is that services don't necessarily fit with what they need."

Dr. Worthington's work is called community-based research. "It's a partnership between academia and the community. Community members and agencies get the information they need to assess services. As an academic, I get rich information about the vulnerable populations I'm interested in. It takes more time to design studies like this, because everyone needs to be at the table to ensure the study asks the questions they want answered. In the end, it's a powerful collaboration with important results."

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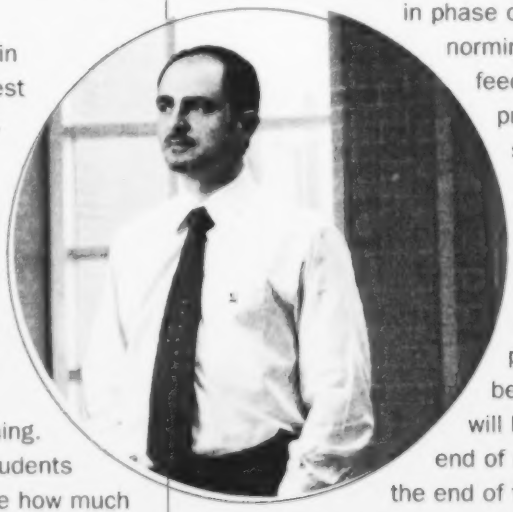
Binge drinking and university students

Binge drinking is the number one health hazard for North American university and college students because of its range of negative consequences—lower marks, run-ins with the law, unwanted or unplanned sex, to name a few. Interventions aimed at bringing it under control have not succeeded in lowering binge-drinking rates.

The University of Calgary's Dr. Shervin Vakili leads a research project to test new techniques to curb binge drinking. The first phase involved an online survey to gather information about student drinking at the University of Calgary. Approximately 2,200 students completed the questionnaire. Now students are being recruited into the second phase of the study, which will test two interventions.

The first intervention is social norming. Based on the finding that university students consistently overestimate how much their peers drink and believe that their peers are more accepting of drinking than they actually are, social norming aims to correct students' misconceptions by giving them information and statistics about drinking behaviour. "The idea is that people increase their drinking to fit the norm," explains Dr. Vakili. "Once you tell them what the norm really is, this should alleviate some of the social pressure and hopefully reduce binge-drinking."

The other intervention adds a personalized feedback message, which tells the individual how much he or she drinks as compared to others (based on the survey data collected in phase one). Both social norming and personalized feedback have shown promise in work with similar groups in the past. All of the information will be distributed to study participants on specially designed postcards. Drinking behaviour and attitudes will be re-assessed at the end of one year and again at the end of the second year.



Dr. Shervin Vakili is an adjunct assistant professor in the Department of Psychology at the University of Calgary, and a psychologist at the Calgary Health Region's Addiction Centre. His study on binge drinking is funded by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

ABOVE: DR. SHERVIN VAKILI

LOOKING AT THE BIG PICTURE

THE GENETIC REVOLUTION has opened up many ethical, legal, and social concerns. The complexity of the questions in these areas, and the lack of clear answers, make the issues very difficult to study. That's not a problem for Heritage Health Scholar Tim Caulfield, research director of the University of Alberta's Health Law Institute and one of the leading researchers in health law in Canada. "The complexity is what makes this whole area so interesting for me," he says.

"IT'S ALL ABOUT PUBLIC TRUST"

Professor Caulfield delves into the ethical, legal, and social issues of genetics and biotechnology through two major research initiatives: Genome Canada, the country's primary funding and information resource relating to genomics and proteomics; and the Stem Cell Network (one of the Networks of Centres of Excellence) which investigates the therapeutic potential of stem cells for the treatment of diseases currently incurable by conventional approaches.

One of his major interests is the commercialization of genetic research. Professor Caulfield is organizing an international workshop in Banff in May to discuss patenting issues. "There are all sorts of recommendations and concerns about patenting genetic material and technologies. We want to look at the available evidence and consider whether the concerns are justified. The workshop will be an excellent forum to determine the current situation. We're also interested in finding out what kinds of evidence are needed. We plan to take information from the workshop, do some of the research, and fill in the gaps, particularly in the Canadian context."

Another area of interest is in the way the media, private companies, and public agencies portray stem-cell and genetic research. "We have a project aimed at getting a sense of the manner in which genetic information is being presented to the public," says Professor Caulfield. One of the aspects he studies is whether the documents take a *genetic essentialist* point of view, reducing the self to a molecular entity and equating human beings—in all their social, historical, and moral complexity—with their genes.

"THE COMPLEXITY IS WHAT MAKES THIS INTERESTING"

As part of his Genome Canada research, Professor Caulfield directs a project that will bring together all the evidence on resource-allocation decisions related to new genetic technologies. His team examines the process of deciding which of these technologies should be funded.

Why bother? It's all about public trust, says Professor Caulfield. "Huge amounts of public money are being invested in genetics and biotechnology. If we're going to do research in these areas, we must ensure that the research is done in a way that maintains public trust."

Dr. Sunita Vohra is an AHFMR Population Health Investigator and associate professor in the Department of Pediatrics with a cross-appointment in the Department of Public Health Sciences at the University of Alberta. She is also director of the Complementary and Alternative Research and Education (CARE) program at the Stollery Children's Hospital and director of the Canadian Pediatric CAM Network. She receives funding from the Canadian Institutes of Health Research (CIHR) and the Institute of Health Economics.

Sabine Moritz is director for research at the Canadian Institute of Natural and Integrative Medicine in Calgary. Her study on spirituality and depression is funded by the Health Research Fund, administered by AHFMR on behalf of Alberta Health and Wellness.

ABOVE: TIM CAULFIELD

Dr. John McLennan is an AHFMR Population Health Investigator, a child psychiatrist, and an assistant professor in the departments of Pediatrics, Community Health Sciences, and Psychiatry at the University of Calgary. He receives funding from CIHR; the Institute of Health Economics; the Alberta Children's Hospital Foundation; the Alberta Centre for Child, Family and Community Research; and the Canadian International Development Agency.

Dr. Catherine Worthington is an AHFMR Population Health Investigator and assistant professor in the Faculty of Social Work at the University of Calgary. She has received funding from SSHRC (Social Sciences and Humanities Research Council of Canada), CIHR, The Ontario HIV Treatment Network, and the Canadian Working Group on HIV and Rehabilitation.

Professor Timothy Caulfield is a full professor in the Faculty of Law and the Faculty of Medicine and Dentistry, and research director of the University of Alberta's Health Law Institute. An AHFMR Health Scholar and Canada Research Chair in Health Law and Policy, his research is supported by Genome Canada, the Stem Cell Network, CIHR, SSHRC, the Advanced Food and Materials Network, and the Alberta Law Foundation.

Selected publications

Moritz S, Quan H, Rickhi B, Liu M, Angen M, Vintila R, Sawa R, Stuart H, Soriano J, Toews J. A home-based spirituality education programme decreases emotional distress and increases quality of life—a randomized controlled trial. *Alternative Therapies in Health and Medicine* 2006. In press 2006.

McLennan JD, MacMillan HL, Jamieson E. Canada's programs to prevent mental health problems in children: the research-practice gap. *Canadian Medical Association Journal* 2004 Oct 26;171(9):1069-1071.

Worthington C, Myers T. Desired elements of HIV testing services: test recipient perspectives. *AIDS Patient Care and STDs* 2002;16(11):537-548.

Caulfield T, Brownsword R. Human dignity: a guide to policy making in the biotechnology era? *Nature reviews, Genetics* 2006 Jan;7(1):72-76.

THE ROAD TO commercialization

An internationally recognized researcher on inflammatory diseases, Heritage Scientist Dr. John Wallace is not used to identifying himself as "the weak link in the chain". But in 2004, when he embarked on commercializing the results of his research, he stepped into a role for which he had no experience or expertise: president and CEO of Antibe Therapeutics Inc.

As the founder of a start-up company with precious little capital, however, Dr. Wallace had no choice but to run Antibe (pronounced "ON-teeb") himself. To bolster his on-the-job learning, Dr. Wallace received help from AHFMR's ForeFront program, which assists Alberta innovators who are commercializing health-related research. ForeFront supports researchers in developing business and entrepreneurial skills through access to expert advice and specialized workshops, and through funding to attend investment conferences. **Page 18 ▸**

ABOVE: DR. ANDRE BURET (L) AND DR. JOHN WALLACE

AHFMR offers Technology Commercialization (TC) project funding in conjunction with the ForeFront program. To date, Antibe has been awarded $685,000 to advance its lead drug to clinical trials.

AHFMR Research News caught up with Dr. Wallace and Dr. Andre Buret, his colleague at the University of Calgary and Antibe's vice-president for basic research, as they were reflecting on some of their experiences to date.

Q **In February 2005 you both attended Invest Northwest in Seattle, the leading investment conference for the life-science community in the Pacific Northwest. Sixty-six companies presented at Invest Northwest 2005; two were from Alberta. You had a twenty-minute opportunity to present your business plan to an international audience of investors. How did it go?**

A *(Dr. Wallace)* I'd never given one of these presentations before. I didn't know what to expect. I'm a scientist, and this is a different pitch. I was the second speaker that morning; the first presenter had organized his talk in a way that was completely opposite to mine. I thought "Uh-oh." But in the end the presentations went well. We got good feedback. We came away feeling good about where our company is.

Q **What did you expect to get out of the conference?**

A *(Dr. Wallace)* I had zero expectations. In terms of attracting funding, I was pretty sure we wouldn't be successful. We're a young company. For venture capitalists, we're premature. We went in with our eyes open. We knew that for what we're selling, probably no one was going to be buying. But it was a good experience. The presentation was good practice. It was a huge plus to see what other companies are doing. The networking was also excellent. Eventually we want to license drugs; so if people say "I've heard of Antibe," that's a good thing. We basically wanted to know: are we really out of our depth or not? This kind of meeting is the best way to get that information.

Q **What kind of lessons did you learn at Invest Northwest?**

A *(Dr. Buret)* The path we've chosen for Antibe is one that's based on scientific evidence. A lot of biotech companies choose the path of commercialization based on marketing, without scientific strength. That's a big difference. We saw some of that in Seattle. I don't think it means that the scientifically based approach is more likely to be successful than the marketing-based one—it's just another path. What I learned is that I'm comfortable with our approach.

A *(Dr. Wallace)* While the experience at Invest Northwest reinforced the idea that having solid science is extremely important, it also demonstrated clearly that to raise money you need an element of showmanship.

Q **Considering that's what sells, how are you adjusting your plans?**

A *(Dr. Wallace)* Well, one of the things I did was fire myself as president. We hired a CEO, Daniel Legault, who has previously served as president of a number of companies. And a CFO, Alain Wilson, who has extensive experience in repositioning, restructuring, and business turnarounds. If I had remained CEO, I would have held the company back; I don't have the business expertise. So Dan

"The path we've chosen for Antibe is based on scientific evidence"

is working on our presentation for future conferencesand he will be the one presenting, not me. He wants just enough science to get their interest, not reams of slides. Whereas my talk at Invest Northwest was probably 40% science, his presentation is more like 25% science, the rest focused on market positioning and financing.

A *(Dr. Buret)* The other thing to remember is that marketing is expensive, money-wise and time-wise. I mean it's a lot of work, especially with very restricted financial means. Also, I'm not comfortable going out there and standing up in front of an audience and telling a story that will be covered by the media as "we found a cure for cancer". I think there are too many people doing that now.

A *(Dr. Wallace)* Publicly traded companies work hard to bolster stock prices. The ones I talked to say they have to issue a press release every six weeks. But after a while you don't get the little blip in the share price, so you have to think of something else to do.

Q **So what has that taught you about going public?**

A *(Dr. Wallace)* From day one, we've known that if we go public, it will be under a CEO who has run a public company. That's when we let go. I have friends who take companies public, and they say "you don't ever want to do this". That's Dan's attitude too. His job as CEO is to get us positioned, and then we'll bring in a CEO who is experienced with public biotech companies.

Q **So this is on your radar screen?**

A *(Dr. Wallace)* Yes, although people tell us to "get acquired before going public". Everything we do now to promote the company positions us for acquisition. However, we are doing some small things in case we decide to go public–for example, having financial statements audited. The point is that we keep both options open. We don't have to select one right now. It's realistic to be flexible.

Q **You took three weeks out of your schedule to take the executive development program at Queen's University. Why?**

A *(Dr. Wallace)* Two reasons; one is historical. After I finished my B.Sc. I got accepted into an MBA program, but I never did it. The itch to do an MBA has always been there, and this program represented a taste of what it would be like. The second is that I felt the need for more basic business skills. It was an incredibly intense three weeks: week 1 is strategy and planning; week 2 is finance and accounting, week 3 is leadership. It was really good, and we had unbelievable teachers.

Q **Are you a better manager now?**

A *(Dr. Wallace)* Yes, I've changed things both in the company and in academia. In particular, I've changed the way I communicate, especially in terms of mentorship, coaching, and active listening. Some of the skills–like negotiating–I haven't had the opportunity to practise yet. But we're going to be licensing a drug soon, so I'll get a chance to do that.

Q **What is holding Antibe back?**

A *(Dr. Wallace)* Our limitations are time and money. If we had more money, we would hire more people. Hiring Dan and Al hasn't given us more time; it just means that collectively we're doing more. They're doing the fundraising and preparing the materials–all that stuff. And Andre and I are doing the science, more of it. There's no question we're getting more science done. Our progress has been substantial.

Q **Has your attitude changed?**

A *(Dr. Wallace)* I think we all have more confidence. Partly because we've had feedback on patents, which we didn't have a year ago. Also, we're just that much more mature as a company. We have a clearer idea of what kind of information we need, and the places to get it. We feel more comfortable talking to people about the company, about potential licensing.

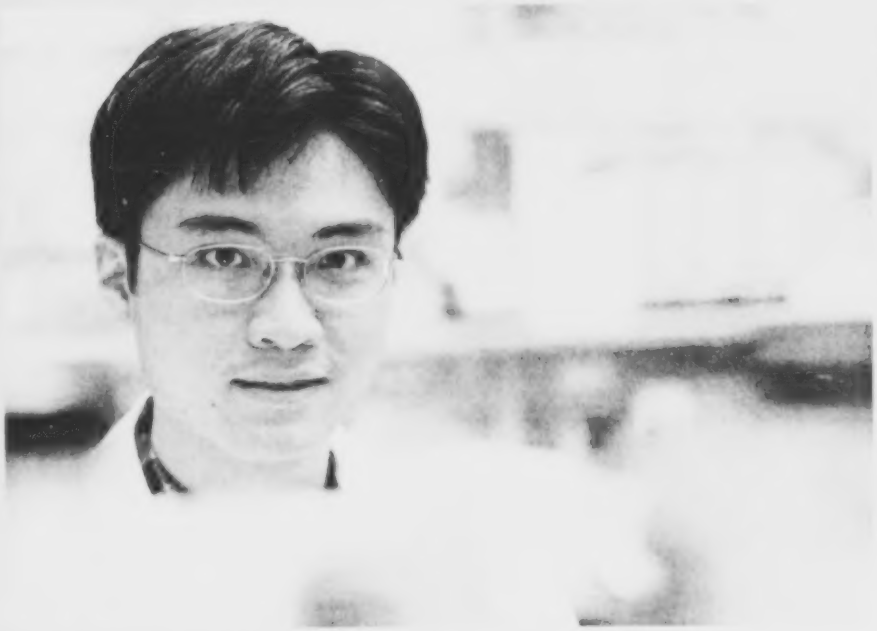
A *(Dr. Buret)* I think our attitude reflects the company's evolution. We've moved from the science, and the excitement of original data, to the company structure and strategic planning of product development. At our scientific advisory board meeting, everyone got together and prioritized what we have in the pipeline. Dan has developed the business plan. We have much more strategy now.

Dr. John Wallace is an AHFMR Scientist and a full professor in both the Department of Pharmacology & Therapeutics and the Department of Physiology & Biophysics at the University of Calgary. He is the chief scientific officer of Antibe Therapeutics Inc.

Dr. Andre Buret is a professor in the Department of Biological Sciences, Faculty of Science, and an adjunct associate professor in the Department of Pharmacology and Therapeutics, Faculty of Medicine, at the University of Calgary, and the vice-president for basic research at Antibe Therapeutics Inc.

ABOVE: DR. ANDRE BURET (L) AND DR. JOHN WALLACE

2005-2006 Lionel McLeod Scholarship winner

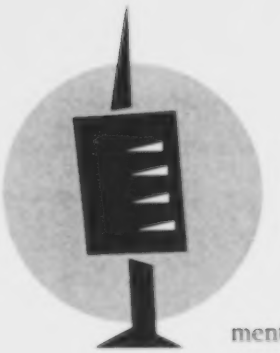


Calvin Yip studies at molecular level how bacterial pathogens cause diseases. More specifically, the winner of the 2005-2006 Lionel E. McLeod Health Research Scholarship investigates a "weapon" that many of these infectious agents use to shoot toxic proteins into our cells. This secretion system, also known as the *molecular syringe* or *molecular needle*, has fascinated the University of British Columbia Ph.D. student since his days as an undergraduate.

Yip uses a method called x-ray crystallography to try to understand how certain bacteria assemble these molecular injection devices. X-ray crystallography is a means of obtaining detailed three-dimensional structural information about very small molecules–so small that they cannot even be examined under a very powerful microscope. "We try to obtain sufficient quantities of the protein or the biological molecule we're interested in and grow crystals of them," says Yip. "These crystals are kind of like diamonds: different molecules packed together in a very ordered manner." Crystallographers then use x-rays to obtain information from these crystals. "Through using different mathematical and computational techniques, you can actually obtain three-dimensional information on biological molecules from subjecting crystals to an x-ray source and collecting diffraction patterns. It's like taking pictures that don't show the actual shape of the object, but depict it as spots."

The molecular syringe plays a central role in the infection process of many pathogens, including *E. coli*, and *Y. pestis* (the bacterium which causes bubonic plague). "These pathogens cause very different diseases but they use a similar way to disrupt normal cell activities," says Yip, explaining that his ultimate goal is to understand how the molecular-syringe mechanism works. "This knowledge could have broad applications because the mechanism is found in so many different pathogens." More knowledge in this area could also lead to the develop-

ABOVE: CALVIN YIP



"It's like taking pictures that depict the object as spots"

ment of new and more effective treatments to battle these dangerous pathogens, which are becoming increasingly resistant to current antibiotics.

After completing his Ph.D., Yip plans to head to Harvard for post-doctoral work in electron microscopy. Electron microscopes can magnify very small details to 500,000 times their actual size through the use of electrons, rather than light, to illuminate material. Yip will study with Dr. Thomas Walz, a world expert in this field. "It's an area which is becoming more popular and more important for studying the structures of bigger and more complicated molecular assemblies," says Yip.

Calvin Yip is currently completing his Ph.D. in the Department of Biochemistry and Molecular Biology at the University of British Columbia. He is the recipient of the 2005-2006 Lionel E. McLeod Health Research Scholarship from AHFMR; he also receives research funding from the Michael Smith Foundation for Health Research.

Thank you

Our thanks to *AHFMR Research News* readers for your overwhelming response to our readership survey. We received 2,700 completed surveys!

Congratulations to the following draw prize winners:

Rex Booth • Calgary, Alberta
Donna Barber • Irma, Alberta
Eugene Topolnisky • Edmonton, Alberta

reader resources

Responding to the reader

Canadian Hemochromatosis Society
http://www.cdnhemochromatosis.ca

Cellular construction

Information on principles of inflammation
http://nic.sav.sk/logos/books/scientific/node5.html

Staying alive

Dr. Michele Barry's website
http://www.ualberta.ca/~mmi/faculty/mbarry/mbarry.html

Howard Hughes Medical Institute
http://www.hhmi.org

Stroke: brain attack

Calgary Stroke Program
http://www.crha-health.ab.ca/stroke/CSPWebPages/

Research outside the lab

The Addiction Centre
http://www.addictioncentre.ca

US National Library of Medicine – MedlinePlus – Alternative Medicine
http://www.nlm.nih.gov/medlineplus/alternaltivemedicine.html

National Center for Complementary and Alternative Medicine (NCCAM) – US National Institutes of Health: Health Information
http://nccam.nih.gov/health/

Longwood Herbal Task Force
http://www.longwoodherbal.org

Canadian Institute of Natural and Integrative Medicine
http://www.cinim.org

AIDS Calgary
http://www.aidscalgary.org

Canadian HIV/AIDS Information Centre
http://www.aidssida.cpha.ca/

University of Alberta Health Law Institute
www.law.ualberta.ca/centres/hli/

Capital Health Weight Wise initiative
http://www.capitalhealth.ca/YourHealth/Campaigns/WeightWise

Dr. Johanne Paradis' website
http://www.ualberta.ca/~jparadis/

The road to commercialization

Antibe Therapeutics
http://www.antibe-therapeutics.com

AHFMR announces $48 million for health research

ABOVE: DR. LORI WEST AND DR. JASON DYCK

Most of us think of heart failure as a disease of aging. Tragically, it can also occur in the tiniest of patients—newborns. Dr. Jason Dyck investigates pediatric cardiac hypertrophy, an abnormal increase in the size of the cells of the heart muscle that can result in heart failure and other heart-related illnesses. Dr. Lori West is a renowned pediatric heart-transplant researcher recently recruited to Edmonton from Toronto. Their work is part of a growing body of expertise in newborn and child health at the University of Alberta.

Ground-breaking research has earned Dr. Dyck and Dr. West funding from the Alberta Heritage Foundation for Medical Research (AHFMR) that will help them improve the health and quality of life of Albertans and people around the world. They are among the 63 researchers in Alberta who have been offered a total of nearly $48 million in AHFMR funding in 2006. This year's recipients also include Dr. Carolyn Emery, a physiotherapist and epidemiologist at the University of Calgary who does research on the prevention of injuries in youth sports such as soccer; and Dr. Robert Sutherland, director of the Canadian Centre for Behavioural Neuroscience at the University of Lethbridge, who studies fetal alcohol syndrome.

AHFMR funding provides salaries, equipment, laboratory start-up, and other support for top health researchers in our province. Over the past 25 years, AHFMR has invested more than $850 million in health research in Alberta. For a complete list of senior personnel awards for 2006, go to **http://www.ahfmr.ab.ca** and click on "AHFMR awards $48 million for research in Alberta".

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Edmonton, Alberta T5J 4A7

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